REMARKS

Claims 1-7, 18 and 29-34 are pending. Claims 1, 2, and 4 have been amended. New claims 29-34 have been added. Support for the new claims can be found in the claims as originally filed and throughout the specification of the present application. No new matter has been added.

Rejection of Claims 1 and 4 Under 35 U.S.C. §112, second paragraph

Claims 1 and 4 are rejected under 35 U.S.C. §112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner states that

> [i]n claim 1 it is not clear what is meant by 'naturally occurring allelic variant'; is the claim referring to variants due to degeneracy of the genetic code and thereby claim nucleic acids that code for the protein of SEQ ID NO:2; or does this also include changes in the protein sequence.

Applicants respectfully traverse this rejection. At the onset, Applicants note that claim 1, as amended, no longer recites this language. This language can be found, however, in new claim 32. Thus, the rejection is addressed below.

The term "naturally occurring allelic variant" is clearly defined in the present application. For example, page 21, lines 28-29 and page 22, lines 1-9 of the present application state that

> [i]n addition to the human COCH5B2 nucleotide sequence shown in SEQ ID NO:1, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of COCH5B2 may exist within a population (e.g., the human population). Such genetic polymorphism in the COCH5B2 gene may exist among individuals within a population due to natural allelic variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding a COCH5B2 protein, preferably a mammalian COCH5B2 protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the COCH5B2 gene. Any and all such nucleotide variations and resulting amino acid polymorphisms in COCH5B2 that are the result of natural allelic variation and that do not alter the functional activity of COCH5B2 are intended to be within the scope of the invention.

Thus, the term "naturally occurring allelic variants" is clearly defined in the present application. Therefore, Applicants respectfully request that the Examiner withdraw this rejection.

The Examiner further states that "[i]n claim 4 it is not clear what is meant by "heterologous polypeptide"; will this just include sequences that are used for protein purification purposes, or does this include fusion with any undisclosed protein that may or may not have therapeutic properties."

Claim 4 has been amended, thereby obviating this rejection.

Rejection of Claim 1 Under 35 U.S.C. §112, first paragraph

Claim 1 is rejected under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention." According to the Examiner,

> [t]he claims are drawn to a naturally occurring allelic variant of SEQ ID NO:2. The specification discloses an isolated cDNA sequence, SEQ ID NO:1, which encodes a predictive polypeptide sequence, SEQ ID NO:2. The broadly claimed allelic variant could include proteins that are functionally similar. The instant disclosure of a single species does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed polypeptide. There is no description of the conserved regions, which are critical to the structure, and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of the structure to function. The structure of these elements is not conventional in the art and a skilled artisan would therefore not recognize from the disclosure that the applicant was in possession of the genus of nucleic acids, representing SEQ ID NO:1. Therefore, there is a lack of sufficient written description in the instant specification for the claimed allelic variants.

Applicants respectfully traverse this rejection. At the onset, Applicants note that claim 1, as amended, is no longer directed towards naturally occurring variants of the sequence encoding COCH5B2. Claim 32, however, recites an isolated nucleic acid molecule which

encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:1 or SEQ ID NO:3 under stringent conditions, and wherein the polypeptide has at least one COCH5B2 activity.

There is clearly sufficient written support in the present application for the claimed variants. For example, at page 21, lines 28-29 and page 22, lines 1-9, the present application provides that

> [i]n addition to the human COCH5B2 nucleotide sequence shown in SEQ ID NO:1, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of COCH5B2 may exist within a population (e.g., the human population). Such genetic polymorphism in the COCH5B2 gene may exist among individuals within a population due to natural allelic variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding a COCH5B2 protein, preferably a mammalian COCH5B2 protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the COCH5B2 gene. Any and all such nucleotide variations and resulting amino acid polymorphisms in COCH5B2 that are the result of natural allelic variation and that do not alter the functional activity of COCH5B2 are intended to be within the scope of the invention.

Moreover, Applicants have provided the nucleic acid sequence encoding human COCH5B2 and have provided description of various domains and conserved amino acids found in the amino acid sequence of human COCH5B2. See e.g., page 14, lines 12-29 and page 15, lines1-27 of the present application. Applicants have also provided various COCH5B2 activities which a variant of COCH5B2 can have. See e.g., page 16, lines 13-20 of the present application. In view of such disclosures, it is clear that there is sufficient written description in the present application for the claimed variants.

Therefore, Applicants respectfully request that the Examiner withdraw this rejection.

Rejection of Claims 1 and 2 Under 35 U.S.C. §102(a)

Claims 1 and 2 are rejected under 35 U.S.C. §102(a) as "being anticipated by Robetson et al. (Genomics, December 1997)." According to the Examiner,

> Roberston et al. discloses GenBank/EMBL submission of sequences AF006741 and AF006740 which are identical matches to SEQ ID NO:1 and 3 of the instant invention. Therefore, the instant invention is anticipated by Robertson et al.

Applicants respectfully request that the Examiner withdraw this rejection in view of the *In re* Katz Declaration by Nahid Robertson, Ph.D. submitted on herewith.

Rejection of Claims 1 and 2 Under 35 U.S.C. §102(a)

Claims 1 and 2 are rejected under 35 U.S.C. §102(a) or 102(b), depending on the date of availability, as being anticipated by sequence AF006741 (GenBank/EMBL, directed submission, 4 June 1997) and sequence AF006740 (GenBank/EMBL, direct submission, 4 June 1997). According to the Examiner,

> The GenBank/EMBL submission discloses sequences AF006741 and AF006740 which are identical matches to SEQ ID NO:1 and 3 of the instant invention. Therefore, the instant invention is anticipated by AF006741 and AF006740.

Applicants respectfully request that the Examiner withdraw this rejection in view of the *In re* Katz Declaration by Nahid Robertson, Ph.D. submitted on herewith. As noted in this Declaration, Applicants submitted GenBank/EMBL Accession Numbers AF006741 and AF006740 prior to the publication of the Robertson et al. reference discussed above, however, these sequences were not made available on GenBank until after the publication of Robertson et al. (1997).

Rejection of Claim 1 Under 35 U.S.C. §102(a)

Claim 1 is rejected under 35 U.S.C. §102(a), as being anticipated by Heller et al. (PNAS, September 1998). According to the Examiner,

> Heller et al. disclose GenBank/EMBL submission AF012252 which contains stretches of nucleic acids that code for greater than 15 contiguous amino acids of SEQ ID NO:2. Therefore, the instant invention is anticipated by Heller et al.

Claim 1, as amended, no longer recites this limitation. Applicants note that new claim 31 recites an isolated nucleic acid molecule which encodes a fragment of a polypeptide of the

listed amino acid sequence, wherein the fragment includes at least 75 contiguous amino acid residues of the amino acid sequence of the listed amino acid sequence.

The GenBank/EMBL submission provided by Heller et al. does not contain a stretch of nucleic acids that code for greater than 75 contiguous amino acids of SEQ ID NO:2. Therefore, Heller et al. does not anticipate the claimed invention.

Rejection of Claim 1 Under 35 U.S.C. §102(a) or 102(b)

Claim 1 is rejected under 35 U.S.C. §102(a) or 102(b), depending on the date of public availability, as being anticipated by sequence AF012252 (GenBank/EMBL, directed submission, 2 July 1997). According to the Examiner,

> The GenBank/EMBL submission discloses sequences AF012252 which contains stretches of nucleic acids that code for greater than 15 contiguous amino acids of SEQ ID NO:2. Therefore, the instant invention is anticipated by sequence AF012252.

As discussed above, claim 1, as amended, no longer recites this limitation. Applicants note that new claim 31 recites an isolated nucleic acid molecule which encodes a fragment of a polypeptide of the listed amino acid sequence, wherein the fragment includes at least 75 contiguous amino acid residues of the amino acid sequence of the listed amino acid sequence.

The GenBank/EMBL submission provided by Heller et al. does not contain a stretch of nucleic acids that code for greater than 75 contiguous amino acids of SEQ ID NO:2. Therefore, Heller et al. does not anticipate the claimed invention.

Thus, Applicants respectfully request that the Examiner withdraw this rejection.

Rejection of Claim 1 Under 35 U.S.C. §102(b)

Claim 1 is rejected under 35 U.S.C. §102(b) as "being anticipated by Robertson et al. (Genomics, 1994)." According to the Examiner,

> Robertson et al. disclose GenBank/EMBL submission of sequence U09203 which contains stretches of nucleic acids that are sufficient to code for greater than 15 contiguous amino acids of SEQ ID NO:2. Therefore, the instant invention is anticipated by Robertson et al.

As discussed above, claim 1, as amended, no longer recites this limitation. Applicants note that new claim 31 recites an isolated nucleic acid molecule which encodes a fragment of a polypeptide of the listed amino acid sequence, wherein the fragment includes at least 75 contiguous amino acid residues of the amino acid sequence of the listed amino acid sequence.

The GenBank/EMBL submission provided by Robertson et al. does not contain a stretch of nucleic acids that code for greater than 75 contiguous amino acids of SEQ ID NO:2. Therefore, Robertson et al. does not anticipate the claimed invention.

Thus, Applicants respectfully request that the Examiner withdraw this rejection.

Rejection of Claim 1 Under 35 U.S.C. §102(b)

Claim 1 is rejected under 35 U.S.C. §102(b) as "being anticipated by VanCollie et al. (Genomics, March 1997)." According to the Examiner,

> Van Collie et al. disclose GenBank/EMBL submission of sequence Z78142 which shares greater than 60% sequence identity with SEQ ID NO:3. Therefore the instant invention is anticipated by VanCollie et al.

Claim 1, as amended, no longer recites this limitation. Applicants note that new claim 34 is directed to an isolated nucleic acid molecule comprising a nucleotide sequence which has at least 90% sequence identity to a nucleotide sequence of SEQ ID NO:3, or a complement thereof..

The sequence provided by VanCollie et al. does not share greater than 90% sequence identity with SEQ ID NO:3. Therefore, VanCollie et al. does not anticipate the claimed invention.

Thus, Applicants respectfully request that the Examiner withdraw this rejection.

Rejection of Claims 1 and 18 Under 35 U.S.C. §103(a)

Claims 1 and 18 are rejected under 35 U.S.C. §103(a0 as being obvious over Robertson et al. (Genomics 1994). In particular, the Examiner states that

> Robertson et al. teach GenBank/EMBL submission AF012252 which contains stretches nucleic acids that are sufficient to code for greater than 15 contiguous amino acids of SEQ ID NO:2. The sequence was used as a probe to detect the distribution of Coch5B2 (see figure 2). The reference does not teach formulating the probe into a kit. It would have been obvious to one of ordinary skill in the art at the time the invention was made to package the probe into a kit for diagnostic purposes. One having ordinary skill in the art would have been motivated to do package the required components into a kit for the sake of conveniently providing the reagents to unskilled personnel. Therefore, the instant invention is obvious over Robertson et al.

As discussed above, claim 1, as amended, no longer recites this limitation. Applicants note that new claim 31 recites an isolated nucleic acid molecule which encodes a fragment of a polypeptide of the listed amino acid sequence, wherein the fragment includes at least 75 contiguous amino acid residues of the amino acid sequence of the listed amino acid sequence.

The GenBank/EMBL submission provided by Robertson et al. does not contain a stretch of nucleic acids that code for greater than 75 contiguous amino acids of SEQ ID NO:2. In addition, Robertson et al. does not teach or suggest a kit which includes a compound which selectively hybridizes to such a nucleic acid molecule. Therefore, Robertson et al. do not render the claimed invention obvious. Thus, Applicants respectfully request that the Examiner withdraw this rejection.

Rejection of Claims 1-7 Under 35 U.S.C.§103(a)

Claims 1-7 are rejected under 35 U.S.C. §103(a) as being "unpatentable over Robertson et al. (Genomic, December 1997) in view of the Pharmacia Catalog (1996). According to the Examiner,

> Robertson teaches the nucleic acid sequences of SEQ ID NO:1 and 3. The references does not teaching inserting the sequences into an expression vector.
>
> It would have been obvious to one of ordinary skill in the art at the time the invention was made to take the nucleic acid sequence as taught by Robertson et al. and insert them into expression vectors in order to produce the encoded polypeptides. Inserting nucleic acid into expression vectors is routine to one of ordinary skill in the art as evidenced by the numerous of prokaryotic and

eukaryotic expression vectors and competent host cells that are commercially available (see Pharmacia Catalog).

Applicants respectfully request that the Examiner withdraw this rejection in view of the *In re* Katz Declaration by Nahid Robertson, Ph.D. submitted on herewith.

Claims 1-7 are also rejected under 35 U.S.C.§103(a) as being unpatentable over VanCollie et al. (Genomics, March 1997), Robertson et al. (Genomics 1994) or Heller et al. (PNAS, September 1998) each in view of the Pharmacia Catalog (1996). In particular, the Examiner states that

> The relevance of the sequences taught by VanCollie et al., Robertson et al. or Heller et al. has been discussed above. It would have been obvious to one of ordinary skill in the art at the time the invention was made to take the nucleic acid sequence as taught by VanCollie et al., Robertson et al. or Heller et al. and insert them into expression vectors in order to produce the encoded polypeptides. Inserting nucleic acid into expression vectors is routine to one of ordinary skill in the art as evidenced by the numerous of prokaryotic and eukaryotic expression vectors and competent host cells that are commercially available (see Pharmacia Catalog).

As discussed throughout this response, none or VanCollie et al., Robertson et al. or Heller et al. teach or suggest the claimed invention. The Pharmacia Catalog does not make up for the deficiencies in these references. Thus, Applicants respectfully request that the Examiner withdraw this rejection.

Conclusion

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be allowed. Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 3/20/01

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Version with markings to show changes made

In the specification:

A paragraph beginning at page 1, line 4 has been added as follows:

-- This application claims the benefit of a previously filed Provisional Application No. 60/102,343, filed September 29, 1998, the contents of which is incorporated in its entirety. --

In the claims:

Claims 1, 2, and 4 have been amended and new claims 29-34 have been added as follows:

1. (Amended) An isolated nucleic acid molecule [selected from the group consisting of:

a) a nucleic acid molecule] comprising a nucleotide sequence which has at least [60%] 85% sequence identity to a nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, or a complement thereof[;

b) a nucleic acid molecule comprising a fragment of at least 1000 nucleotides of a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, or a complement thereof;

c) a nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence having at least about [60%] 85% sequence identity to the amino acid sequence of SEQ ID NO:2;

d) a nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the fragment comprises at least [15] 75 contiguous amino acid residues of the amino acid sequence of SEQ ID NO:2; and

e) a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:1 or SEQ ID NO:3 under stringent conditions].

2. (Amended) [The] An isolated nucleic acid molecule [of claim 1 which is selected from the group consisting of:

a) a nucleic acid molecule] comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, or a complement thereof[; and

b) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2].

4. (Amended) The nucleic acid molecule of claim 1 further comprising nucleic acid sequences encoding a [heterologous] non-COCH5B2 polypeptide.

--29. (New) An isolated nucleic acid molecule comprising a fragment of at least 1000 nucleotides of a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, or a complement thereof.

30. (New) An isolated nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO:2.

31. (New) An isolated nucleic acid molecule comprising which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the fragment comprises at least 75 contiguous amino acid residues of the amino acid sequence of SEQ ID NO:2.

32. (New) An isolated nucleic acid molecule comprising which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:1 or SEQ ID NO:3 under stringent conditions, and wherein the polypeptide has at least one COCH5B2 activity.

33. (New) An isolated nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2.

34. (New) An isolated nucleic acid molecule comprising a nucleotide sequence which has at least 90% sequence identity to a nucleotide sequence of SEQ ID NO:3, or a complement thereof.--